

Human pluripotent stem cell-based therapeutics for preeclampsia

Grant Award Details

Human pluripotent stem cell-based therapeutics for preeclampsia

Grant Type: New Faculty Physician Scientist

Grant Number: RN3-06396

Project Objective: To establish in vitro models for the study of pre-eclampsia and to screen for small molecules that reverse the disease phenotype in those models. The in vitro model will consist of hPSC-derived extravillous trophoblasts (EVT) derived from hPSC-derived cytotrophoblasts (CTB).

Investigator:

Name:	Mana Parast
Institution:	University of California, San Diego
Type:	PI

Disease Focus: Fertility

Human Stem Cell Use: iPS Cell

Cell Line Generation: iPS Cell

Award Value: \$2,974,750

Status: Active

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 2

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Reporting Period: Year 3

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Grant Application Details

Application Title: Human pluripotent stem cell-based therapeutics for preeclampsia

Public Abstract: Preeclampsia (PE) is a pregnancy complication, characterized by high blood pressure and abnormal kidney function, which affects 5-8% of all pregnancies. It is responsible for a significant proportion of maternal deaths and growth-restricted babies; it is also a major reason why obstetricians induce delivery prematurely, resulting in additional neonatal complications, often requiring extended stays in neonatal intensive care units. PE is a disease of the placenta, an organ which supports the fetus during intrauterine life. In PE, a subpopulation of placental cells called "extravillous trophoblast" (EVT) fail to properly develop: in their absence, the placenta does not receive enough blood supply and therefore cannot support fetal growth. PE is difficult to study: it spontaneously develops only in higher primates, and available human trophoblast cell lines are of limited use. Using normal human ES-derived trophoblast precursors, we propose to screen for drugs which can increase EVT differentiation. We will also apply stem cell-based technology to cells from placentas of PE patients, in order to develop "disease-in-a-dish" models for PE. We will then test the ability of the drugs, identified above, to restore EVT differentiation in these PE models. If successful, this application will 1) establish the first true cell culture model for preeclampsia, and 2) identify drugs for its treatment.

Statement of Benefit to California: On an average day in California, 149 babies are born prematurely. Many of these babies will require weeks of care in a neonatal intensive care unit, at an average per patient cost of \$25,000 (compared to the \$1,500 per patient cost of a baby born at term). The #1 reason obstetricians induce preterm delivery is a disease called preeclampsia, where mom develops high blood pressure and other serious complications during pregnancy. Preeclampsia is also responsible for ~20% of maternal deaths in pregnancy. Preeclampsia is not well-understood, but is known to be a disease of the placenta, an organ which forms the interface between mother and baby. Our lab is one of few in the world that focuses on stem cells which give rise, not to the baby, but to the placenta: these are called trophoblast stem cells. We have recently developed a human trophoblast stem cell model, which can be used to study events during placental development, never before possible in the human. This proposal, if funded, would extend these findings to develop ground-breaking models for studying preeclampsia and identifying drugs for its treatment. If successful, this research would benefit the state of California by developing therapies which would prevent preeclampsia, and therefore a significant proportion of preterm births and its complications. This would lead, not only to improved health of moms and babies, but also save the state millions in cost of prolonged stays in neonatal intensive care units.

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